

#### APPENDIX E: Scientific Abstract

Gaucher's disease is the most frequent sphingolipid storage disorder and affects about 30,000 patients in the United States. It is an autosomal recessive hereditary deficiency of a lysosomal enzyme, glucocerebrosidase, required for glycolipid degradation. The absence of a functional glucocerebrosidase leads to accumulation of glucosylcerebroside in macrophages throughout the reticular endothelial system. This lipid storage typically leads to hepatosplenomegaly, hypersplenism and lytic bone lesions.

The purpose of this study is to investigate whether ex vivo retrovirus-mediated transfer of the cDNA for human glucocerebrosidase into peripheral blood repopulating cells of patients with Type 1 Gaucher's disease followed by infusion of the transduced cells into the patient is safe and able to improve or cure the disease. Peripheral blood repopulating cells will be mobilized by treatment of the patient with recombinant human granulocyte colony-stimulating factor collected by repeated leukapheresis and selected for CD34 positive cells by avidin-biotin-immunoabsorption. CD34 positive cells will then be transduced ex vivo over a 5-day period in a long-term marrow culture system containing medium with retrovirus supernatant. After transduction, cells will be infused into the patient without myeloablative treatment. Collection, transduction and infusion of transduced peripheral blood cells will be repeated two times at 2-month intervals to increase the amount of transduced repopulating cells transplanted.

The primary endpoint of this study is to examine the safety of infusing peripheral blood repopulating cells transduced with the human glucocerebrosidase cDNA. The persistence and expression of the glucocerebrosidase gene in hematopoietic cells after infusion will also be studied.